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Applicants

Schreiber & Crabtree

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For

Methods and Materials Involving Dimerization-Mediated Regulation of Biological Events

Assistant Commissioner for Patents Washington, DC 20231

November 7, 2001

Response to Notice to File Corrected Application Papers, Amendment & Petition for 3-Month Extension of time

This is in response to the 6/8/01 Notice to File Corrected Application Papers, a response to which was originally due on 8/8/01. Applicants hereby petition for a three-month extension of time and authorize the PTO to charge our Deposit Account 01-2315 the required \$460.00 fee, as well as any other fee which may be due at this time in connection with this matter. Accordingly, this Response should be considered timely filed.

Amendment

Drawings and Brief Description of the Drawings

Please delete the 11 lines of text at the bottom of Fig 7 and insert the following into the Brief Description of the Drawings for Fig 7, beginning at the end of line 24, page 6:

-- The receptor binding domain can be identified by inspection of the receptor coding sequence (e.g. Kyte Doolittle analysis) or by analysis of deletion mutants (see Watowich et al, Mol. Cell. Biol. 14:3535 1994). PCR primers flanking the LIGAND BINDING DOMAIN are used to PCR amplify the region encoding the LBD. By inclusion of sequences encoding a particular epitope in the other PCT primer, an epitope can be fused to the N- or C-terminus of the LBD. Other PCT primers can be used to introduce restriction sites into the ends of the LBD coding sequence to facilitate cloning. The cloned LBD is then ligated into an appropriate expression vector, such as the pcDNA series from Invitrogen, Inc. for mammalian cell expression. To express a receptor immunoglobulin fusion protein, the amplified LBD segment is ligated into an expression vector containing the hinge, CH2 and CH3 domains of an IgG heavy chain as described in Ashkenazi et al, PNAS 88:10535 1991. See e.g., Nature 330, 537-543 (1987) for details relevant to GH receptor. --

This amendment corrects minor errors in the text from Fig 7 and moves the corrected text to the specification. This amendment does not introduce any new matter.

Attached hereto is a marked-up version of the change made by the current amendment. The attached page is entitled "Black-Lined Version Of Amended Section Showing Change Made."

Respectfully submitted,

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I hereby certify that this paper is being deposited on November 7, 2001 with the United States Postal Service, as First Class Mail with sufficient postage, and is addressed to Assistant Commissioner for Patents, Washington, DC 20231 pursuant to 37 CFR 1.10

Signed See Leslan Date 11.7-01

Black-Lined Version of Amended Section Showing Change Made

page 6, line 24 ...:

Fig 7 depicts a general methodology for the design and construction of an expression vector for producing a portion of a receptor protein, *e.g.*, for use in binding experiments. The receptor binding domain can be identified by inspection of the receptor coding sequence (e.g. Kyte Doolittle analysis) or by analysis of deletion mutants (see Watowich et al, Mol. Cell. Biol. 14:3535 1994). PCR primers flanking the LIGAND BINDING DOMAIN are used to PCR amplify the region encoding the LBD. By inclusion of sequences encoding a particular epitope in the other PCT primer, an epitope can be fused to the N- or C-terminus of the LBD. Other PCT primers can be used to introduce restriction sites into the ends of the LBD coding sequence to facilitate cloning. The cloned LBD is then ligated into an appropriate expression vector, such as the pcDNA series from Invitrogen, Inc. for mammalian cell expression. To express a receptor immunoglobulin fusion protein, the amplified LBD segment is ligated into an expression vector containing the hinge, CH2 and CH3 domains of an IgG heavy chain as described in Ashkenazi et al, PNAS 88:10535 1991. See e.g., Nature 330, 537-543 (1987) for details relevant to GH receptor.